REMARKS

Claims 1-17 are pending in the instant application. Claims 1-17 have been rejected. Claim 1 has been amended. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims 1, 11 and 13 under 35 U.S.C. § 102(b)

Claims 1, 11 and 13 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Wallace et al. (Protein Science (June 1996) 5:1001-1013). Arguments presented in the previous response submitted by Applicants on June 13, 2001, including a Declaration by an inventor, were not found persuasive as the Examiner suggests that the different feature by which Applicants distinguish their invention, namely the size of the protein domain, is not distinct from the teaching of Wallace which shows a three dimensional putative polypeptide domain which is comprised of the entire polypeptide, or at least 195 amino acids. Applicants respectfully traverse this rejection.

At the outset, the claims have been amended in order to make it clear that the claims of the instant invention are identifying a polypeptide domain that is limited to a size of from 50 to 300 amino acids. This is very different from the method taught by

Wallace et al. (1996). The paper by Wallace et al. (1996) teaches derivation of 3-dimensional coordinate templates that have been derived from known 3-dimensional protein structures that are provided in a database and then determination of biochemical function based on the existence of known 3-dimensional structures. This method is based on identification of a triad (i.e., three, amino acids, Ser-His-Asp) that occur in a 3-dimensional configuration to form an active site. Nowhere does this paper teach or suggest identifying a protein domain by identifying the presence of more than these three amino acids. A declaration was provided in the previous response dated June 13, 2001 by Dr. Montelione, a co-inventor in the instant application affirming the validity of this interpretation of the teachings of Wallace et al. (1996). In this declaration, the numbering of the amino acids and a determination of how many amino acids have been identified is clarified and the teachings of the Wallace reference clearly distinguished. It is important to note that the reference of Wallace et al. does limit itself to identifying polypeptide domains strictly by the presence of the triads described. Nowhere does this paper teach or suggest that there would be a size limitation of a stable polypeptide domain such as now claimed in the instant invention. Contrary to the examiner's suggestion, Wallace et al.

does **not** teach, that there may be **any** size range to a stable domain. It only teaches identifying domains in general through identifying the triads. Further, as stated in the paper of Wallace et al. at page 1011, second column, first full paragraph, "In this paper, we have only dealt with the Ser-His-Asp catalytic triad..."; this statement demonstrate that the authors have not contemplated any other size domain. The fact the authors have limited themselves to this size range also supports the view that it would not be obvious for one of skill to attempt to identify larger domains and to be assured that the larger size domain would be a tool for determining function or structure of a protein. Accordingly, the reference of Wallace et al. fails to teach the limitations of the invention as claimed and cannot anticipate the presently claimed invention.(MPEP 2131). Withdrawal of this rejection is respectfully requested.

II. Rejection of Claims Under 35 U.S.C. § 103(a)

Claims 1, 5-9, 11 and 13 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Wallace et al. in view of Friedrichs et al. (J. Biomol. NMR (1994) 4:703-726). Claims 1-9, 11, 13 and 14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. in view of Friedrichs et al. and

further in view of Farber et al. (J. Mol. Biol. (1992) 226:471-479). In addition, claims 1, 5-11 and 13 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Wallace et al. in view of Friedrichs et al. and further in view of Bagby et al. (J. Biomol. NMR (1997) 10:279-282). Finally, claims 1-9 and 11-17 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Wallace et al. in view of Friedrichs et al. and further in view of Farber et al. (J. Mol. Biol. (1992) 226:471-479) and further in view of Orengo et al. (Structure (August 1997) 5:1093-1108). Applicants respectfully traverse each rejection of the claims under 35 U.S.C. 103(a).

MPEP § 2143 states that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references when combined must teach or suggest all the claim limitations.

As discussed in Section I, *supra*, the primary reference by Wallace et al. does not teach the identification of protein domains of 50 to 300 amino acids. Nor is there any suggestion of this step

as Wallace et al. teaches identification of a domain based on the presence of triads of amino acids. Accordingly, the primary reference fails to teach or suggest all the limitations as now claimed. This reference is common to each of the rejections cited.

The secondary references cited under 35 U.S.C. 103(a) fail to overcome the deficiencies in teaching of this primary reference.

The teachings of Friedrichs et al. are related to an automated system for protein ^{15}N, ^{13}C, and ^{1}H NMR resonance assignments from a set of three-dimensional NMR spectra. This reference provides no teaching or suggestion of identifying a putative polypeptide domain that properly folds into a stable polypeptide domain of 50 to 300 amino acids as claimed.

Farber et al. disclose a neural network and information theory for determination of coding regions of DNA sequences. This reference also contains no teaching or suggestion with respect to identification of protein or polypeptide domains of 50 to 300 amino acids.

Similarly references by Bagby et al. and Orengo et al. fail to teach or suggest this claim limitation. As acknowledged by the Examiner, the teachings of Bagby et al. are related to preparation of samples for NMR analysis while the teachings of Orengo et al.

are limited to the use of the CATH method for classification of protein domains.

Both the MPEP and the case law are clear; to establish *prima facie* obviousness of a claimed invention, all the limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974) and MPEP § 2143.03. Accordingly, since none of the prior art references teach or suggest the limitation of identifying a putative polypeptide domain of 50 to 300 amino acids that properly folds into a stable polypeptide domain of 50 to 300 amino acids, the cited combinations of prior art cannot render obvious the invention as set forth in claim 1 or claims dependent therefrom.

Withdrawal of these rejections under 35 U.S.C. § 103(a) is therefore respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The

attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 1 has been amended as follows:

1. (amended) A high-throughput method for determining a biochemical function of a protein or polypeptide domain of unknown three dimensional structure and function comprising:

(A) identifying a putative polypeptide domain consisting of 50 to 300 amino acids that properly folds into a stable polypeptide domain consisting of 50 to 300 amino acids;

(B) determining three dimensional structure of the stable polypeptide domain;

(C) comparing the determined three dimensional structure of the stable polypeptide domain to known three-dimensional structures in a protein data bank, wherein said comparison identifies known structures within said protein data bank that are homologous to the determined three dimensional structure; and

(D) correlating a biochemical function corresponding to the identified homologous structure to a biochemical function for the stable polypeptide domain.